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# Effectiveness of oral propranolol in a patient with neurofibromatosis type 1 and infantile hemangiomas.

emanuele MIRAGLIA, amalia SCHIAVETTI, giulia VARRASSO, mauro CELLI, Stefano CALVIERI, Sandra GIUSTINI

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**Title:** Effectiveness of oral propranolol in a patient with neurofibromatosis type 1 and infantile hemangiomas.

#### **Contributors:**

Emanuele Miraglia\*, <sup>1</sup> Amalia Schiavetti, <sup>2</sup> Giulia Varrasso, <sup>2</sup> Mauro Celli, <sup>2</sup> Stefano Calvieri, <sup>1</sup> Sandra Giustini. <sup>1</sup>

#### **Affiliations:**

- Department of Dermatology and Venereology, "Sapienza" University of Rome, Policlinico Umberto I, Viale del Policlinico, 155 Rome, Italy.
- Department of Pediatrics, "Sapienza" University of Rome, Policlinico Umberto I, Viale del Policlinico, 155 Rome, Italy.

### **Corresponding author:**

Dr. Emanuele Miraglia; Department of Dermatology and Venereology, "Sapienza" University of Rome, Viale del Policlinico, N.155, 00161, Rome, Italy. Tel. +390649976968; Fax +390649976907; e-mail: emanuele.miraglia@hotmail.it.

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Dear editor,

Neurofibromatosis type I (NF1) is an inherited autosomal dominant condition which affects approximately one in 2500 to one in 3000 people. In about 50% of individuals, the disease is caused by a spontaneous mutation and in the other 50%, the disease is inherited.

The NF1 gene maps on chromosome 17q11.2 and encodes the protein neurofibromin, which has a role in tumor suppression and the disease involves aberrant proliferation of multiple tissues of neural crest origin. NF1 is characterized by a predisposition to the development of benign and malignant tumors.<sup>1</sup>

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy, with a reported incidence of approximately 5%. IHs occur more frequently in female infants; prematurity, low birth weight and placental anomalies appear to be the most significant risk factors with a 40% increase in risk for every 500 gram decrease in birth weight.<sup>2</sup>

The natural history of IH is characterized by a rapid proliferative phase during early infancy, from birth to approximately 1 year of age, followed by a gradual involution that may last until the age of 10 years. Some IHs can present serious complications and cosmetic disfigurement, causing functional and psychological effects on parents and the affected children.<sup>3</sup> Early treatment can control the growth of tumors and accelerate the involution, avoid leaving scar which affect appearance. Various systemic and topical therapies have been studied in the treatment of IHs.

Propranolol has been demonstrated to be a well-tolerated medication, with effectiveness in all stages, both halting growth during the proliferative phase as well as hastening the involution phase.<sup>4,5</sup>

We report the case of a 4 month old female child with NF1 and IH treated with systemic propranolol.

At the general clinical examination, the patient showed 15 café-au lait spots. She had also a nodular lesion of red violet color, soft in consistency, located on the trunk, appeared a few days after birth

(Figure 1a). No sign of ulceration was evident. The ultrasound examination showed intense vascularization.

Family history was positive for NF1 (mother) but was negative for hemangiomas. On the basis of these findings, were made diagnosis of NF1 and IH.

We performed a cardiological examination with electrocardiogram and blood pressure measurement that resulted within the standards. A pediatric hematochemical examination to evaluate the liver and kidney function was also performed providing results within the standard.

We decided to start treatment with propranolol beginning with a minimum dose of 1 mg/kg/day in order to get to the final dose of 2 mg/Kg/day in 2 doses a day. No adverse effects were reported.

After 9 months, we noticed a considerable reduction of the lesion (Figure 1b).

Patients with NF1 are at increased risk of developing many neoplasms, approximately four times higher than general population matched for age and gender, particularly neoplasia originated from the neural crest derivatives.<sup>1</sup> IHs are the most common tumor of childhood. The pathogenesis has not yet been fully elucidated. At present, there are three main hypotheses: the theory of tissue hypoxia, the theory of embolization of placental endothelial cells, and the theory of increased angiogenic and vasculogenic activity.

HIs of the trunk have been rarely treated with oral propranolol because this type of IH is not included in the group for which such therapy is justified. In our case we decided to treat this IH because it was large and could bleed with trauma.

The association between NF1 and IH, observed in the present report, have not been described earlier. We cannot exclude that the such association is a coincidental finding. However, neurofibromin could play a role in the pathogenesis of IH like in other tumors.

We report this case to emphasize the peculiarity of this rare association and to underline the efficacy and safety of propranolol treatment for IHs also in genodermatosis such as NF1.

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Figure 1 (a). Infantile hemangiomas pre-treatment.

Figure 1 (b). Infantile hemangiomas post-treatment with considerable reduction of the lesion.





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